

inducible upstream activating sequence, 2) a minimal promoter sequence and 3) 5' and 3' P transposable elements;

(c) producing progeny from the breeding of the first *D. melanogaster* with the second *D. melanogaster*;

(d) screening the progeny for increased or decreased polyglutamine toxicity relative to the first *D. melanogaster* thereby identifying a progeny having increased or decreased polyglutamine toxicity; and

(e) identifying one or more genes operationally-associated with the marker sequence, or having an insertion of the marker sequence, that confers increased or decreased polyglutamine toxicity in the progeny having increased or decreased polyglutamine toxicity.

10. (Twice Amended) The method of claim 1, wherein the second *D. melanogaster* is selected from a group of two or more animals having markers inserted into different locations of its genomic DNA.

11. (Twice Amended) The method of claim 10, wherein the second *D. melanogaster* is selected from a group of 10 to 100, 100 to 500, or 500 or more of the animals.

12. (Twice Amended) The method of claim 1, wherein the second *D. melanogaster* is selected from a library of animals having markers inserted at random locations of their genomic DNA.

13. (Twice Amended) The method of claim 12, wherein the library is generated by random P element insertion.

25. (Twice Amended) A progeny *D. melanogaster* produced by the method of claim 1.

B³
26. (Twice Amended) A transgenic *D. melanogaster* comprising a transgene containing a plurality of CAG's and at least one CAA sequence encoding a polyglutamine repeat sequence, wherein the repeat comprises at least 100 contiguous glutamine residues.

B⁴
29. (Twice Amended) The *D. melanogaster* of claim 26, wherein the number of CAG's to CAA's is in ratio of between about 1:1 and 2:1.

30. (Twice Amended) The *D. melanogaster* of claim 26, wherein the number of CAG's to CAA's is in ratio of between about 2:1 and 5:1.

31. (Twice Amended) The *D. melanogaster* of claim 26, wherein the number of CAG's to CAA's is in ratio of between about 5:1 and 10:1.

32. (Twice Amended) The *D. melanogaster* of claim 26, wherein the number of CAG's to CAA's is in ratio of between about 10:1 and 50:1.

33. (Twice Amended) The *D. melanogaster* of claim 26, wherein expression of the polyglutamine sequence is conferred by a constitutive, regulatable or tissue specific expression control element.

34. (Twice Amended) The *D. melanogaster* of claim 33, wherein the tissue specific expression control element confers neural, retinal, muscle or mesoderm cell expression.

35. (Twice Amended) The *D. melanogaster* of claim 33, wherein the tissue specific expression control element comprises an Appl or rhodopsin 1 promoter or GLASS transcription factor element.

By 36. (Twice Amended) The *D. melanogaster* of claim 26, wherein the polyglutamine sequence is between about 30 and 50 amino acids in length.

37. (Twice Amended) The *D. melanogaster* of claim 26, wherein the polyglutamine sequence is between about 50 and 100 amino acids in length.

38. (Twice Amended) The *D. melanogaster* of claim 26, wherein the polyglutamine sequence is between about 100 and 200 amino acids in length.

39. (Twice Amended) The *D. melanogaster* of claim 26, wherein the polyglutamine sequence is between about 50 and 200 amino acids in length.

40. (Twice Amended) The *D. melanogaster* of claim 26, wherein the polyglutamine sequence further comprises a tag.

41. (Twice Amended) The *D. melanogaster* of claim 26, wherein polyglutamine toxicity is produced in one or more tissue or organs of the animal.

34 42. (Twice Amended) The *D. melanogaster* of claim 26, wherein the *Drosophila* further comprises a marker sequence inserted into its genomic DNA, wherein the marker is located adjacent to a gene or inserted into a gene whose expression or activity increases or decreases polyglutamine toxicity in the animal, and wherein the marker sequence comprises an inducible upstream activating sequence, a minimal promoter sequence and 5' and 3' P transposon elements containing terminal inverted repeats.

43. (Twice Amended) The *D. melanogaster* of claim 42, wherein the marker sequence is near or inserted into a gene containing a J domain.

44. (Twice Amended) The *D. melanogaster* of claim 43, wherein the gene is HDJ1.

45. (Twice Amended) The *D. melanogaster* of claim 43, wherein the gene is TPR2.

46. (Twice Amended) The *D. melanogaster* of claim 43, wherein the marker sequence is near an MLF gene.

35 50. (Twice Amended) A method of producing a transgenic *D. melanogaster* characterized by suppressed polyglutamine toxicity comprising:

(a) transforming a *D. melanogaster* embryo or fertilized egg with a transgene comprising a plurality of CAA and CAG sequences encoding a polyglutamine sequence comprising at least 100 contiguous glutamine residues; and

Applicant: Parsa Kazemi-Esfarjani et al.
Serial No.: 09/639,207
Filed : August 14, 2000
Page : 6

Attorney's Docket No.: 06618-686001 / CIT-3056

(b) selecting a *D. melanogaster* that exhibits
polyglutamine toxicity.

Ob
view
